AT-NO: 6001577
MENT-IDENTIFIER: US 6001577 A

TLE: Systematic evolution of ligands by exponential enrichment: photoselection of nucleic acid ligands and solution selex

DATE-ISSUED: December 14, 1999

INVENTOR-INFORMATION: NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Larry	Boulder	CO	N/A	N/A
Willis; Michael	Louisville	CO	N/A	N/A
Koch; Tad	Boulder	CO	N/A	N/A
Ringquist; Steven	Lyons	CO	N/A	N/A
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US-CL-CURRENT: 435/6; 435/91.2, 536/25.4

CLAIMS:

We claim:
1. A method for identifying a nucleic acid ligand to a target molecule that is associated with a disease state in a biological substance, said method comprising:

a) identifying a nucleic acid ligand that photocrosslinks to a target molecule from a candidate mixture of nucleic acids, wherein each member of said candidate mixture contains a photoreactive group, said method comprising:
i) contacting said candidate mixture of nucleic acids with a first biological substance which contains a target molecule that is associated with said disease state, wherein nucleic acids having an increased affinity to a molecule of said first biological substance relative to the candidate mixture form nucleic acid-molecule complexes with said molecule;
ii) irradiating said complexes, wherein said nucleic acid and molecule photocrosslink;
iii) partitioning the photocrosslinked nucleic acid-molecule complexes from the remainder of the candidate mixture; and
iv) identifying nucleic acid ligands that photocrosslink to said target molecule;
b) contacting a second biological substance which does not contain said target molecule that is associated with said disease state with said nucleic acid ligands identified in step iv), wherein the nucleic acids with affinity to a molecule that is not associated with the disease state in the second biological substance is removed; and
c) amplifying the remaining nucleic acids with specific affinity to said target molecule that is associated with a disease state to yield a mixture of nucleic acids enriched for nucleic acids with relatively higher affinity and specificity for binding to said target molecule that is associated with said disease state, whereby a nucleic acid ligand to a target molecule that is associated with a disease state in a biological substance is identified.
2. The method of claim 1 further comprising after step iv);
v) repeating steps i) through iii); and
vi) amplifying the nucleic acids that photocrosslinked to the target molecule that is associated with a disease state.

3. The method of claim 1 wherein said biological substance is serum.
4. The method of claim 1 wherein said target molecule is selected from the group consisting of a protein, peptide, carbohydrate, polysaccharide, glycoprotien, hormone, receptor, antigen, antibody, virus, substrate, metabolite, transition state analog, cofactor, inhibitor, drug, dye, nutrient, and growth factor.
5. The method of claim 4 wherein said target molecule that is associated with a disease state is a protein.
6. The method of claim 4 wherein said protein is alpha-foeto protein.
7. The method of claim 1 wherein said photoreactive group is selected from the group consisting of 5-bromouracil, 5-iodouracil, 5-bromovinyluracil, 5-iodovinyluracil, 5-azidouracil, 4-thiouracil, 5-bromocytosine, 5-iodocytosine, 5-bromovinylcytosine, 5-iodovinylcytosine, 5-azidocytosine, 8-azidoadenine, 8-bromoadenine, 8-iodoadenine, 8-azidoguanine, 8-bromoguanine, 8-iodoguanine, 8-azidohypoxanthine, 8-bromohypoxanthine, 8-iodohypoxanthine, 8-azidoxanthine, 8-bromoxanthine, 8-iodoxanthine, 5-bromodeoxyuracil, 8-bromo-2'-deoxyadenine, 5-iodo-2'-deoxyuracil, 5-iodo-2'-deoxycytosine, 5-[(4-azidophenacyl)thio]cytosine, 5-[(4-azidophenacyl)thio]uracil, 7-deaza-7-iodoadenine, 7-deaza-7-iodoguanine, 7-deaza-7-bromoadenine, and 7-deaza-7-bromoguanine.
8. The method of claim 1 wherein the photocrosslinking nucleic acid ligand comprises one or more photoreactive groups, and wherein said photoreactive group is selected from the group consisting of 5-bromouracil, 5-iodouracil, 5-bromovinyluracil, 5-iodovinyluracil, 5-azidouracil, 4-thiouracil, 5-bromocytosine, 5-iodocytosine, 5-bromovinylcytosine, 5-iodovinylcytosine, 5-azidocytosine, 8-azidoadenine, 8-bromoadenine, 8-iodoadenine, 8-azidoguanine, 8-bromoguanine, 8-iodoguanine, 8-azidohypoxanthine, 8-bromohypoxanthine, 8-iodohypoxanthine, 8-azidoxanthine, 8-bromoxanthine, 8-iodoxanthine, 5-bromodeoxyuracil, 8-bromo-2'-deoxyadenine, 5-iodo-2'-deoxyuracil, 5-iodo-2'-deoxycytosine, 5-[(4-azidophenacyl)thio]cytosine, 5-[(4-azidophenacyl)thio]uracil, 7-deaza-7-iodoadenine, 7-deaza-7-iodoguanine, 7-deaza-7-bromoadenine, and 7-deaza-7-bromoguanine.
9. A method for identifying a nucleic acid ligand to a target molecule that is associated with a disease state in a biological substance, said method comprising:

a) identifying a nucleic acid ligand that photocrosslinks to a target molecule from a candidate mixture of nucleic acids, said method comprising:
i) contacting said candidate mixture of nucleic acids with a first biological substance which contains a target molecule that is associated with said disease state, wherein nucleic acids having an increased affinity to a molecule of said first biological substance relative to the candidate mixture form nucleic acid-molecule complexes with said molecule;
ii) partitioning the complexed increased affinity nucleic acids from the remainder of the candidate mixture;
iii) amplifying the increased affinity nucleic acids to yield a ligand-enriched mixture of nucleic acids,
iv) incorporating photoreactive groups into said amplified increased affinity nucleic acids;
v) irradiating said increased affinity nucleic acids, wherein said nucleic acid-molecule complexes photocrosslink;
vi) partitioning the photocrosslinked nucleic acid-molecule complexes from the remainder of the candidate mixture; and
vii) identifying nucleic acid ligands that photocrosslink to the molecule;
b) contacting a second biological substance which does not contain said target molecule that is associated with said disease with said nucleic acid ligands identified in step vii), wherein the nucleic acids with affinity to a molecule that is not associated with said disease is removed; and
c) amplifying the remaining nucleic acids with specific affinity to said target molecule that is associated with said disease state to yield a mixture of nucleic acids enriched for nucleic acids with relatively higher affinity and specificity for binding to said target molecule that is associated with said disease state, whereby nucleic acid ligands to a target molecule that is associated with a disease state in a biological substance is identified.
10. The method of claim 9 further comprising:
d) repeating step i); and
e) repeating steps iii) and iv).
11. The method of claim 9 wherein said biological substance is serum.
12. The method of claim 9 wherein said target molecule that is associated with a disease state is selected from the group consisting of protein, peptide, carbohydrate, polysaccharide, glycoprotien, hormone, receptor, antigen, antibody, virus, substrate, metabolite, transition state analog, cofactor, inhibitor, drug,

dye, nutrient, and growth factor.
13. The method of claim 12 wherein said target molecule that is associated with a disease state is a protein.
14. The method of claim 13 wherein said protein is alpha-foeto protein.
15. The method of claim 9 wherein said photoreactive group is selected from the group consisting of 5-bromouracil, 5-iodouracil, 5-bromovinyluracil, 5-iodovinyluracil, 5-azidouracil, 4-thiouracil, 5-bromocytosine, 5-iodocytosine, 5-bromovinylcytosine, 5-iodovinylcytosine, 5-azidocytosine, 8-azidoadenine, 8-bromoadenine, 8-iodoadenine, 8-azidoguanine, 8-bromoguanine, 8-iodoguanine, 8-azidohypoxanthine, 8-bromohypoxanthine, 8-iodohypoxanthine, 8-azidoxanthine, 8-bromoxanthine, 8-iodoxanthine, 5-bromodeoxyuracil, 8-bromo-2'-deoxyadenine, 5-iodo-2'-deoxyuracil, 5-iodo-2'-deoxycytosine, 5-[(4-azidophenacyl)thio]cytosine, 5-[(4-azidophenacyl)thio]uracil, 7-deaza-7-iodoadenine, 7-deaza-7-iodoguanine, 7-deaza-7-bromoadenine, and 7-deaza-7-bromoguanine.
16. The method of claim 9 wherein the photocrosslinking nucleic acid ligand comprises one or more photoreactive groups, and wherein said photoreactive group is selected from the group consisting of 5-bromouracil, 5-iodouracil, 5-bromovinyluracil, 5-iodovinyluracil, 5-azidouracil, 4-thiouracil, 5-bromocytosine, 5-iodocytosine, 5-bromovinylcytosine, 5-iodovinylcytosine, 5-azidocytosine, 8-azidoadenine, 8-bromoadenine, 8-iodoadenine, 8-azidoguanine, 8-bromoguanine, 8-iodoguanine, 8-azidohypoxanthine, 8-bromohypoxanthine, 8-iodohypoxanthine, 8-azidoxanthine, 8-bromoxanthine, 8-iodoxanthine, 5-bromodeoxyuracil, 8-bromo-2'-deoxyadenine, 5-iodo-2'-deoxyuracil, 5-iodo-2'-deoxycytosine, 5-[(4-azidophenacyl)thio]cytosine, 5-[(4-azidophenacyl)thio]uracil, 7-deaza-7-iodoadenine, 7-deaza-7-iodoguanine, 7-deaza-7-bromoadenine, and 7-deaza-7-bromoguanine.

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L17: Entry 1 of 1 File: USPT Dec 7, 1999

US-PAT-NO: 5998142
DOCUMENT-IDENTIFIER: US 5998142 A

TITLE: Systematic evolution of ligands by exponential enrichment: chemi-SELEX

DATE-ISSUED: December 7, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Larry	Boulder	CO	N/A	N/A
Eaton; Bruce	Boulder	CO	N/A	N/A
Smith; Drew	Boulder	CO	N/A	N/A
Wecker; Matthew	Boulder	CO	N/A	N/A
Jensen; Kirk	New York	NY	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.2, 536/23.1, 536/24.3, 536/25.4

CLAIMS:

We claim:
1. Nucleic acid ligands that bind covalently with a protein, wherein said nucleic acid ligands comprise a chemically reactive functional unit, wherein said nucleic acid ligands are produced by the method comprising the steps of:
a) preparing a candidate mixture of nucleic acids;
b) contacting the candidate mixture with said protein, wherein nucleic acids which bind covalently with said protein may be partitioned from the remainder of the candidate mixture;
c) partitioning the nucleic acids that bind covalently with the protein from the remainder of the candidate mixture; and
d) amplifying the nucleic acids that bind covalently with the protein, whereby nucleic acid ligands that bind covalently with the protein may be produced.
2. The nucleic acid ligands of claim 1 which are selected from the sequences listed in Table VI (SEQ ID NOS: 108-224).
3. A facilitating nucleic acid, wherein said nucleic acid comprises a chemically reactive functional unit, identified according to the method comprising the steps of:
a) preparing a candidate mixture of nucleic acids;
b) contacting the candidate mixture with a protein, wherein nucleic acids having a facilitating activity, as indicated by a covalent bond being formed between said protein and said nucleic acid, relative to the candidate mixture may be partitioned from the remainder of the candidate mixture;
c) partitioning the nucleic acids having a facilitating activity from the remainder of the candidate mixture; and
d) amplifying the nucleic acids having a facilitating activity, whereby a facilitating nucleic acid may be identified.
4. A method for partitioning nucleic acids from a nucleic acid candidate mixture, wherein said nucleic acid ligands comprise a chemically reactive functional unit, said method comprising:
a) preparing a nucleic acid candidate mixture;
b) contacting the nucleic acid candidate mixture with a protein under conditions wherein nucleic acids form a covalent bond with said protein; and
c) partitioning away the remainder of the nucleic acid candidate mixture which did not form a covalent bond with the protein, leaving only nucleic acids which have formed a covalent bond with the protein.

formed a covalent bond with the protein.
5. A purified and isolated non-naturally occurring nucleic acid ligand which binds covalently with a protein, wherein said nucleic acid ligand comprises a chemically reactive functional unit.

col 10 l 25-27 cr Pu incl photoreactive grps.

+ see Ex 4 - col 29.
photo-SELEX → 5-iodouracil

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L19: Entry 1 of 1 File: USPT Oct 5, 1999

US-PAT-NO: 5962219
DOCUMENT-IDENTIFIER: US 5962219 A

TITLE: Systematic evolution of ligands by exponential enrichment: chemi-selex

DATE-ISSUED: October 5, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Larry	Boulder	CO	N/A	N/A
Eaton; Bruce	Boulder	CO	N/A	N/A
Smith; Drew	Boulder	CO	N/A	N/A
Wecker; Matthew	Boulder	CO	N/A	N/A
Jensen; Kirk	Boulder	CO	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.2, 536/24.31, 536/25.4

CLAIMS:

We claim:
1. A method for identifying nucleic acids having a facilitating activity from a candidate mixture comprised of nucleic acids wherein each nucleic acid has at least one nucleic acid region and at least one chemically reactive functional unit which binds covalently with a target, said method comprising:
a) contacting the candidate mixture with said target, wherein nucleic acids having a facilitating activity, as indicated by a covalent bond being formed between said target and said chemically reactive functional unit of said nucleic acid, may be partitioned from the remainder of the candidate mixture; and
b) partitioning the nucleic acids having a facilitating activity from the remainder of the candidate mixture, whereby nucleic acids having a facilitating activity are identified.
2. The method of claim 1 wherein after step b), the nucleic acids having a facilitating activity are amplified and steps a) and b) are repeated.
3. The method of claim 1 wherein said chemically reactive functional unit is selected from the group consisting of photoreactive groups, active site directed compounds and peptides.
4. The method of claim 1 wherein the target is modified to include a chemical moiety that reacts with the chemically reactive functional unit of the nucleic acid.
5. The method of claim 1 wherein said nucleic acid comprises a fixed region and a randomized region.
6. The method of claim 5 wherein said at least one chemically reactive functional unit is attached to an oligonucleotide hybridized to said fixed region.

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L20: Entry 3 of 3 File: USPT Jun 9, 1998

US-PAT-NO: 5763595
DOCUMENT-IDENTIFIER: US 5763595 A

TITLE: Systematic evolution of ligands by exponential enrichment: Chemi-SELEX

DATE-ISSUED: June 9, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Larry	Boulder	CO	N/A	N/A
Eaton; Bruce	Boulder	CO	N/A	N/A
Smith; Drew	Boulder	CO	N/A	N/A
Wecker; Matthew	Boulder	CO	N/A	N/A
Jensen; Kirk	Boulder	CO	N/A	N/A

US-CL-CURRENT: 536/22.1; 435/6, 435/91.2, 536/25.4

CLAIMS:

We claim:
1. Nucleic acid ligands which bind covalently with a protein, wherein said nucleic acid ligands comprise a chemically reactive functional unit selected from the group consisting of pohotoreactive groups and active site directed compounds, wherein said nucleic acid ligands are produced by a method comprising the steps of:
a) preparing a candidate mixture of nucleic acids;
b) contacting said candidate mixture with said protein, wherein nucleic acids which bind covalently with said protein may be partitioned from the remainder of said candidate mixture;
c) partitioning the nucleic acid-protein complexes from free nucleic acids in said candidate mixture; and
d) identifying said nucleic acid ligands that bind covalently with said protein.
2. The nucleic acid ligands of claim 1 which are selected from the sequences listed in Tables II and IV.
3. The nucleic acid ligand of claim 1 wherein said nucleic acids comprise a fixed sequence region.
4. The nucleic acid ligand of claim 3 wherein at least one fuinctional unit is attached to an oligonucleotide hybridized to said fixed sequence region.
5. A purified and non-naturally occurring nucleic acid ligand which binds covalently with a protein, wherein said nucleic acid ligand comprises a chemically reactive functional unit selected from the group comprising photoreactive groups and active site directed compounds.

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End of Result Set

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L18: Entry 13 of 13 File: USPT Jun 9, 1998

US-PAT-NO: 5763177
DOCUMENT-IDENTIFIER: US 5763177 A

TITLE: Systematic evolution of ligands by exponential enrichment: photoselection of nucleic acid ligands and solution selex

DATE-ISSUED: June 9, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Larry	Boulder	CO	N/A	N/A
Willis; Michael	Louisville	CO	N/A	N/A
Koch; Tad	Boulder	CO	N/A	N/A
Ringquist; Steven	Lyons	CO	N/A	N/A
Jensen; Kirk	Boulder	CO	N/A	N/A
Atkinson; Brent	Boulder	CO	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.2, 536/23.1, 536/25.4

CLAIMS:

We claim:
1. A method for identifying a nucleic acid ligand that photocrosslinks to a protein from a candidate mixture of nucleic acids, wherein each member of said candidate mixture contains a photoreactive group, said method comprising:
a) contacting said candidate mixture with said protein, wherein nucleic acids having an increased affinity to the protein relative to the candidate mixture form nucleic acid-protein complexes with the protein;
b) irradiating said complexes, wherein said nucleic acid-protein photocrosslink;
c) partitioning the photocrosslinked nucleic acid-protein complexes from in the candidate mixture; and
d) identifying a nucleic acid ligand that photocrosslinked to the protein.
2. The method of claim 1 further comprising after step c):
i) repeating steps a) through c); and
ii) amplifying the nucleic acids that photocrosslinked to the protein.
3. The method of claim 1 wherein after step c) the protein is removed from the nucleic acid-protein complex by proteolytic digestion.
4. The method of claim 1 wherein said identified nucleic acid ligand modifies a biological activity of said protein.
5. A method for identifying a photocrosslinking nucleic acid ligand of a protein from a candidate mixture of nucleic acids, said method comprising:
a) contacting said candidate mixture with said protein, wherein nucleic acids having increased affinity to the protein relative to the candidate mixture form nucleic acid-protein complexes with the protein;
b) partitioning the complexed increased affinity nucleic acids from the remainder of the candidate mixture;
c) amplifying the increased affinity nucleic acids to yield a ligand-enriched mixture of nucleic acids;
d) incorporating photoreactive groups into said amplified increased affinity nucleic acids;
e) repeating step;
f) irradiating said increased affinity nucleic acids, wherein said nucleic acid-protein complexes photocrosslink;

g) repeating steps c) and d); and
h) identifying a photocrosslinking nucleic acid ligand to the protein.
6. The method of claim 1 for identifying a nucleic acid ligand that photocrosslinks to a protein further comprising the steps:
e) preparing a second candidate mixture of nucleic acids from the nucleic acid ligand identified in step d):
f) contacting said second candidate mixture with said protein wherein nucleic acids having an increased affinity to the protein relative to the second candidate mixture form nucleic acid-protein complexes:
g) partitioning the increased affinity nucleic acids from the remainder of the second candidate mixture, and
h) amplifying the increased affinity nucleic acids to yield a ligand-enriched mixture of nucleic acids whereby a nucleic acid ligand that photocrosslinks the protein is identified.
7. The method of claim 1 wherein said photoreactive group is selected from the group consisting of 5-bromouracil, 5-iodouracil, 5-bromovinyluracil, 5-iodovinyluracil, 5-azidouracil, 4-thiouracil, 5-bromocytosine, 5-iodocytosine, 5-bromovinylcytosine, 5-iodovinylcytosine, 5-azidocytosine, 8-azidoadenine, 8-bromoadenine, 8-iodoadenine, 8-azidoguanine, 8-bromoguanine, 8-iodoguanine, 8-azidohypoxanthine, 8-bromohypoxanthine, 8-iodohypoxanthine, 8-azidoxanthine, 8-bromoxanthine, 8-iodoxanthine, 5-bromodeoxyuracil, 8-bromo-2'-deoxyadenine, 5-iodo2'-deoxyuracil, 5-iodo-2'-deoxycytosine, 5-[(4-azidophenacyl)thio]cytosine, 5-[(4-azidophenacyl)thio]uracil, 7-deaza-7-iodoadenine, 7-deaza-7-iodoguanine, 7-deaza-7-bromoadenine, and 7-deaza-7-bromoguanine.
8. The method of claim 1 wherein the photocrosslinking nucleic acid ligand comprises one or more photoreactive groups, and wherein said photoreactive group is selected from the group consisting of 5-bromouracil, 5-iodouracil, 5-bromovinyluracil, 5-iodovinyluracil, 5-azidouracil, 4-thiouracil, 5-bromocytosine, 5-iodocytosine, 5-bromovinylcytosine, 5-iodovinylcytosine, 5-azidocytosine, 8-azidoadenine, 8-bromoadenine, 8-iodoadenine, 8-aziodoguanine, 8-bromoguanine, 8-iodoguanine, 8-azidohypoxanthine, 8-bromohypoxanthine, 8-iodohypoxanthine, 8-azidoxanthine, 8-bromoxanthine, 8-iodoxanthine, 5-bromodeoxyuracil, 8-bromo-2'-deoxyadenine, 5-iodo-2'-deoxyuracil, 5-iodo-2'-deoxycytosine, 5-[(4-azidophenacyl)thio]cytosine, 5-[(4-azidophenacyl)thio]uracil, 7-deaza-7-iodoadenine, 7-deaza-7-iodoguanine, 7-deaza-7-bromoadenine, and 7-deaza-7-bromoguanine.
9. The method of claim 6 wherein the photocrosslinking nucleic acid ligand comprises one or more photoreactive groups, and wherein said photoreactive group is selected from the group consisting of 5-bromouracil, 5-iodouracil, 5-bromovinyluracil, 5-iodovinyluracil, 5-azidouracil, 4-thiouracil, 5-bromocytosine, 5-iodocytosine, 5-bromovinylcytosine, 5-iodovinylcytosine, 5-azidocytosine, 8-azidoadenine, 8-bromoadenine, 8-iodoadenine, 8-aziodoguanine, 8-bromoguanine, 8-iodoguanine, 8-azidohypoxanthine, 8-bromohypoxanthine, 8-iodohypoxanthine, 8-azidoxanthine, 8-bromoxanthine, 8-iodoxanthine, 5-bromodeoxyuracil, 8-bromo-2'-deoxyadenine, S-iodo-2'-deoxyuracil, 5-iodo-2'-deoxycytosine, 5-[(4-azidophenacyl)thio]cytosine, 5-[(4-azidophenacyl)thio]uracil, 7-deaza-7-iodoadenine, 7-deaza-7-iodoguanine, 7-deaza-7-bromoadenine, and 7-deaza-7-bromoguanine.
10. The method of claim 6 wherein the photocrosslinking nucleic acid ligand comprises one or more photoreactive groups, and wherein said photoreactive group is selected from the group consisting of 5-bromouracil, 5-iodouracil, 5-bromovinyluracil, 5-iodovinyluracil, 5-azidouracil, 4-thiouracil, 5-bromocytosine, 5-iodocytosine, 5-bromovinylcytosine, 5-iodovinylcytosine, 5-azidocytosine, 8-azidoadenine, 8-bromoadenine, 8-iodoadenine, 8-aziodoguanine, 8-bromoguanine, 8-iodoguanine, 8-azidohypoxanthine, 8-bromohypoxanthine, 8-iodohypoxanthine, 8-azidoxanthine, 8-bromoxanthine, 8-iodoxanthine, 5-bromodeoxyuracil, 8-bromo-2'-deoxyadenine, 5-iodo-2'-deoxyuracil, 5-iodo-2'-deoxycytosine, 5-[(4-azidophenacyl)thio]cytosine, 5-[(4-azidophenacyl)thio]uracil, 7-deaza-7-iodoadenine, 7-deaza-7-iodoguanine, 7-deaza-7-bromoadenine, and 7-deaza-7-bromoguanine.
11. A nucleic acid ligand that photocrosslinks to a protein, wherein said nucleic acid ligand is comprised of a non-naturally occurring nucleic acid having a specific binding affinity for a protein, wherein said protein is not a nucleic acid binding protein, and wherein said nucleic acid ligand is not a nucleic acid having the known physiological function of being bound by the protein, obtained by the process of identifying a nucleic acid ligand of a protein from a candidate mixture of nucleic acids comprised of nucleic acids each having a region of randomized sequence, and wherein each member of said candidate mixture contains a photoreactive group, said method comprising:

a) contacting said candidate mixture with said protein, wherein nucleic acids having an increased affinity to the protein relative to the candidate mixture form nucleic acid-protein complexes with the protein;
b) irradiating said candidate mixture, wherein said nucleic acidprotein complexes photocrosslink;
c) partitioning the photocrosslinked nucleic acid-protein complexes from the candidate mixture; and
d) identifying a nucleic acid ligand that photocrosslinked to the protein.
12. A nucleic acid ligand of claim 11 further comprising one or more of the photoreactive groups selected from the group consisting of 5-bromouracil, 5-iodouracil, 5-bromovinyluracil, 5-iodovinyluracil, 5-azidouracil, 4-thiouracil, 5-bromocytosine, 5-iodocytosine, 5-bromovinylcytosine, 5-iodovinylcytosine, 5-azidocytosine, 8-azidoadenine, 8-bromoadenine, 8-iodoadenine, 8-aziodoguanine, 8-bromoguanine, 8-iodoguanine, 8-azidohypoxanthine, 8-bromohypoxanthine, 8-iodohypoxanthine, 8-azidoxanthine, 8-bromoxanthine, 8-iodoxanthine, 5-bromodeoxyuracil, 8-bromo-2'-deoxyadenine, 5-iodo-2'-deoxyuracil, 5-iodo-2'-deoxycytosine, 5-[(4-azidophenacyl)thio]cytosine, 5-[(4-azidophenacyl)thio]uracil, 7-deaza-7-iodoadenine, 7-deaza-7-iodoguanine, 7-deaza-7-bromoadenine, and 7-deaza-7-bromoguanine.
13. A nucleic acid ligand that photocrosslinks to a protein, wherein said nucleic acid ligand is comprised of a non-naturally occurring nucleic acid having a specific binding affinity for a protein, wherein said protein is not a nucleic acid binding protein, and wherein said nucleic acid ligand is not a nucleic acid having the known physiological function of being bound by the protein, obtained by the process of identifying a nucleic acid ligand of a protein, from a candidate mixture of nucleic acids comprised of nucleic acids each having a region of randomized sequence, and wherein each member of said candidate mixture contains a photoreactive group, said method comprising:
a) contacting said candidate mixture with said protein, wherein nucleic acids having increased affmity to the protein relative to the candidate mixture form nucleic acid-protein complexes with the protein;
b) partitioning the increased affinity nucleic acids from the remainder of the candidate mixture;
c) amplifying the increased affinity nucleic acids to yield a ligand-enriched mixture of nucleic acids, whereby a nucleic acid ligand of the protein may be identified;
d) incorporating photoreactive groups into said increased affinity nucleic acids;
e) repeating step a);
f) irradiating said increased affinity nucleic acids, wherein said nucleic acid-protein complexes photocrosslink;
g) repeating step c) and d); and
h) identifying a photocrosslinking nucleic acid ligand to the protein.
14. A nucleic acid ligand of claim 13 further comprising one or more of the photoreactive groups selected from the group consisting of 5-bromouracil, 5-iodouracil, 5-bromovinyluracil, 5-iodovinyluracil, 5-azidouracil, 4-thiouracil, 5-bromocytosine, 5-iodocytosine, 5-bromovinylcytosine, 5-iodovinylcytosine, 5-azidocytosine, 8-azidoadenine, 8-bromoadenine, 8-iodoadenine, 8-aziodoguanine, 8-bromoguanine, 8-iodoguanine, 8-azidohypoxanthine, 8-bromohypoxanthine, 8-iodohypoxanthine, 8-azidoxanthine, 8-bromoxanthine, 8-iodoxanthine, 5-bromodeoxyuracil, 8-bromo-2'-deoxyadenine, 5-iodo-2'-deoxyuracil, 5-iodo-2'-deoxycytosine, 5-[(4-azidophenacyl)thio]cytosine, 5-[(4-azidophenacyl)thio]uracil, 7-deaza-7-iodoadenine, 7-deaza-7-iodoguanine, 7-deaza-7-bromoadenine, and 7-deaza-7-bromoguanine.
15) A nucleic acid ligand that photocrosslinks to a protein, wherein said nucleic acid ligand is comprised of a non-naturally occurring nucleic acid having a specific binding affinity for a protein, wherein said protein is not a nucleic acid binding protein and wherein said nucleic acid ligand is not a nucleic acid having the known physiological function of being bound by the protein, obtained by the process of identifying a nucleic acid ligand of a protein from a candidate mixture of nucleic acids comprised of nucleic acids each having a region of randomized sequence, and wherein each member of said candidate mixture contains a photoreactive group, said method comprising:
a) contacting said candidate mixture with said protein, wherein nucleic acids having an increased affinity to the protein relative to the candidate mixture form nucleic acid-protein complexes with the protein;
b) irradiating said candidate mixture, wherein said nucleic acidprotein complexes photocrosslink;
c) partitioning the photocrosslinked nucleic acid-protein complexes from in the candidate mixture;

d) identifying a nucleic acid ligand that photocrosslinked to the protein;.
e) preparing a second candidate mixture of nucleic acids from those nucleic acid ligands identified in step d);
f) contacting said second candidate mixture with said protein, wherein nucleic acids having an increased affinity to the protein relative to the second candidate mixture form nucleic acid-protein complexes with the protein;
g) partitioning the increased affinity nucleic acids from the remainder of the second candidate mixture; and
h) amplifying the increased affinity nucleic acids to yield a ligandenriched mixture of nucleic acids, whereby a nucleic acid ligand that photocrosslinks the protein is identified.

16. A nucleic acid ligand of claim 15 further comprising one or more of the photoreactive groups selected from the group consisting of 5-bromouracil, 5-iodouracil, 5-bromovinyluracil, 5-iodovinyluracil, 5-azidouracil, 4-thiouracil, 5-bromocytosine, 5-iodocytosine, 5-bromovinylcytosine, 5-iodovinylcytosine, 5-azidocytosine, 8-azidoadenine, 8-bromoadenine, 8-iodoadenine, 8-aziodoguanine, 8-bromoguanine, 8-iodoguanine, 8-azidohypoxanthine, 8-bromohypoxanthine, 8-iodohypoxanthine, 8-azidoxanthine, 8-bromoxanthine, 8-iodoxanthine, 5-bromodeoxyuracil, 8-bromo-2'-deoxyadenine, 5-iodo-2'-deoxyuracil, 5-iodo-2'-deoxycytosine, 5-[(4-azidophenacyl)thio]cytosine, 5-[(4-azidophenacyl)thio]uracil, 7-deaza-7-iodoadenine, 7-deaza-7-iodoguanine, 7-deaza-7-bromoadenine, and 7-deaza-7-bromoguanine.

09/723,718

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DB Name	Query	Hit Count	Set Name
USPT	l14 not l10	0	L15
USPT	azidouracil same crosslink$ same nucleic	2	L14
USPT	l12 not l10	4	L13
USPT	iodouracil same crosslink same nucleic	6	L12
USPT	azidocytosine same crosslink same nucleic	0	L11
USPT	bromouracil same crosslink same nucleic	2	L10
USPT	l7 same coat$	12	L9
USPT	l7 same nucleic	0	L8
USPT	silane with functional adj2 group with carboxy?	99	L7
USPT	silane with funcational adj2 group with carboxy?	0	L6
USPT	l1 same immobiliz$	0	L5
USPT	l1 same oligonucleotide	0	L4
USPT	l1 same dna	0	L3
USPT	l1 same nucleic	0	L2
USPT	silane with carboxy? with functional	132	L1

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Search Results - Record(s) 1 through 2 of 2 returned.

☐ 1. Document ID: US 6001577 A

L10: Entry 1 of 2 File: USPT Dec 14, 1999

US-PAT-NO: 6001577
DOCUMENT-IDENTIFIER: US 6001577 A

TITLE: Systematic evolution of ligands by exponential enrichment: photoselection of nucleic acid ligands and solution selex

DATE-ISSUED: December 14, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Larry	Boulder	CO	N/A	N/A
Willis; Michael	Louisville	CO	N/A	N/A
Koch; Tad	Boulder	CO	N/A	N/A
Ringquist; Steven	Lyons	CO	N/A	N/A
Jensen; Kirk	Boulder	CO	N/A	N/A
Atkinson; Brent	Boulder	CO	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.2, 536/25.4

ABSTRACT:

A method for identifying nucleic acid ligands to target molecules using the SELEX procedure wherein the candidate nucleic acids contain photoreactive groups and nucleic acid ligands identified thereby are claimed. The complexes of increased affinity nucleic acids and target molecules formed in the procedure are crosslinked by irradiation to facilitate separation from unbound nucleic acids. In other methods partitioning of high and low affinity nucleic acids is facilitated by primer extension steps as shown in the figure in which chain termination nucleotides, digestion resistant nucleotides or nucleotides that allow retention of the cDNA product on an affinity matrix are differentially incorporated into the cDNA products of either the high or low affinity nucleic acids and the cDNA products are treated accordingly to amplification, enzymatic or chemical digestion or by contact with an affinity matrix.

16 Claims, 29 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 35

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 2. Document ID: US 5763177 A

L10: Entry 2 of 2 File: USPT Jun 9, 1998

US-PAT-NO: 5763177
DOCUMENT-IDENTIFIER: US 5763177 A

TITLE: Systematic evolution of ligands by exponential enrichment: photoselection of nucleic acid ligands and solution selex

DATE-ISSUED: June 9, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Larry	Boulder	CO	N/A	N/A
Willis; Michael	Louisville	CO	N/A	N/A
Koch; Tad	Boulder	CO	N/A	N/A
Ringquist; Steven	Lyons	CO	N/A	N/A
Jensen; Kirk	Boulder	CO	N/A	N/A
Atkinson; Brent	Boulder	CO	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.2, 536/23.1, 536/25.4

ABSTRACT:

A method for identifying nucleic acid ligands to target molecules using the SELEX pocedure wherein the candidate nucleic acids contain photoreactive groups and nucleic acid ligands identified thereby are claimed. The complexes of increased affinity nucleic acids and target molecules formed in the procedure are crosslinked by irradiation to facilitate separation from unbound nucleic acids. In other methods partioning of high and low affinity nucleic acids is facilitated by primer extension steps as shown in the figure in which chain termination nucleotides, digestion resistant nucleotides or nucleotides that allow retention of the cDNA product on an affinity matrix are differentially incorporated into the cDNA products of either the high or low affinity nucleic acids and the cDNA products are treated accordingly to amplification, enzymatic or chemical digestion or by contact with an affinity matrix.

16 Claims, 29 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 35

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Search Results - Record(s) 1 through 4 of 4 returned.

☐ 1. Document ID: US 5998142 A

L13: Entry 1 of 4 File: USPT Dec 7, 1999

US-PAT-NO: 5998142
DOCUMENT-IDENTIFIER: US 5998142 A

TITLE: Systematic evolution of ligands by exponential enrichment: chemi-SELEX

DATE-ISSUED: December 7, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Larry	Boulder	CO	N/A	N/A
Eaton; Bruce	Boulder	CO	N/A	N/A
Smith; Drew	Boulder	CO	N/A	N/A
Wecker; Matthew	Boulder	CO	N/A	N/A
Jensen; Kirk	New York	NY	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.2, 536/23.1, 536/24.3, 536/25.4

ABSTRACT:

This application provides methods for identifying nucleic acid ligands capable of covalently interacting with targets of interest. The nucleic acids can be associated with various functional units. The method also allows for the identification of nucleic acids that have facilitating activities as measured by their ability to facilitate formation of a covalent bond between the nucleic acid, including its associated functional unit, and its target.

5 Claims, 0 Drawing figures Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Drawn Desc | Image

☐ 2. Document ID: US 5962219 A

L13: Entry 2 of 4 File: USPT Oct 5, 1999

US-PAT-NO: 5962219
DOCUMENT-IDENTIFIER: US 5962219 A

TITLE: Systematic evolution of ligands by exponential enrichment: chemi-selex

DATE-ISSUED: October 5, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Larry	Boulder	CO	N/A	N/A
Eaton; Bruce	Boulder	CO	N/A	N/A
Smith; Drew	Boulder	CO	N/A	N/A
Wecker; Matthew	Boulder	CO	N/A	N/A
Jensen; Kirk	Boulder	CO	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.2, 536/24.31, 536/25.4

ABSTRACT:

This application provides methods for identifying nucleic acid ligands capable of covalently interacting with targets of interest. The nucleic acids can be associated with various functional units. The method also allows for the identification of nucleic acids that have facilitating activities as measured by their ability to facilitate formation of a covalent bond between the nucleic acid, including its associated functional unit, and its target.

6 Claims, 0 Drawing figures Exemplary Claim Number: 1

☐ 3. Document ID: US 5763595 A

L13: Entry 3 of 4 File: USPT Jun 9, 1998

US-PAT-NO: 5763595
DOCUMENT-IDENTIFIER: US 5763595 A

TITLE: Systematic evolution of ligands by exponential enrichment: Chemi-SELEX

DATE-ISSUED: June 9, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Larry	Boulder	CO	N/A	N/A
Eaton; Bruce	Boulder	CO	N/A	N/A
Smith; Drew	Boulder	CO	N/A	N/A
Wecker; Matthew	Boulder	CO	N/A	N/A
Jensen; Kirk	Boulder	CO	N/A	N/A

US-CL-CURRENT: 536/22.1; 435/6, 435/91.2, 536/25.4

ABSTRACT:

This application provides methods for identifying nucleic acid ligands capable of covalently interacting with targets of interest. The nucleic acids can be associated with various functional units. The method also allows for the identification of nucleic acids that have facilitating activities as measured by their ability to facilitate formation of a covalent bond between the nucleic acid, including its associated functional unit, and its target.

5 Claims, 0 Drawing figures Exemplary Claim Number: 1

☐ 4. Document ID: US 5705337 A

L13: Entry 4 of 4 File: USPT Jan 6, 1998

US-PAT-NO: 5705337
DOCUMENT-IDENTIFIER: US 5705337 A

TITLE: Systematic evolution of ligands by exponential enrichment: chemi-SELEX

DATE-ISSUED: January 6, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Larry	Boulder	CO	N/A	N/A
Eaton; Bruce	Boulder	CO	N/A	N/A
Smith; Drew	Boulder	CO	N/A	N/A
Wecker; Matthew	Boulder	CO	N/A	N/A
Jensen; Kirk	Boulder	CO	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.2

ABSTRACT:

This application provides methods for identifying nucleic acid ligands capable of covalently interacting with targets of interest. The nucleic acids can be associated with various functional units. The method also allows for the identification of nucleic acids that have facilitating activities as measured by their ability to facilitate formation of a covalent bond between the nucleic acid, including its associated functional unit, and its target.

7 Claims, 0 Drawing figures Exemplary Claim Number: 1